Diagnostic and prognostic significance of complete blood count parameters in retrocecal appendicitis

Significance of complete blood count parameters in retrocecal appendicitis

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Abstract

Aim: Acute appendicitis (AA) is the most common cause of acute abdomen requiring surgery. Because of the difficulty in diagnosing retrocecal appendicitis, complication rates are quite high. In the present retrospective study, we investigated the diagnostic and prognostic significance of complete blood count (CBC) parameters in the diagnosis of retrocecal appendicitis.

Materials and Methods: This study enrolled 48 patients with antececal AA, 36 with retrocecal AA, and 42 controls between July 2016 and 2019. Patients were divided into groups based on the imaging results and the position of the appendix during the operation. The control group consisted of patients who had presented to the emergency room with nonspecific abdominal pain.

Results: No differences were observed between the antececal and retrocecal appendicitis groups regarding all tests. CRP levels were significantly higher in the gangrenous appendicitis group (p=0.038), and its sensitivity and specificity were 41.67% and 100%, respectively. Neutrophil-to-lymphocyte ratio (NLR) was higher in the gangrenous appendicitis group, albeit not statistically significant (p=0.072). CRP was higher in the perforated appendicitis group, though not statistically significant (p=0.066). Mean NLR and platelet-to-lymphocyte ratio (PLR) were significantly higher in the perforated appendicitis group (p=0.003 for NLR and p=0.001 for PLR), and their sensitivities and specificities were 80%, 80%, 90.32%, and 100%, respectively.

Discussion: CBC parameters can be used to diagnose acute appendicitis but cannot help with differentiating antececal and retrocecal appendicitis. Notably, in retrocecal appendicitis, while CRP and NLR could help in detecting gangrenous histopathology, NLR and PLR can help detect perforated appendicitis.

Keywords

Acute appendicitis; Complication; CRP; Neutrophil-to-lymphocyte ratio; Platelet-to-lymphocyte ratio

Introduction

Acute appendicitis (AA) is the most common cause of acute abdomen requiring immediate surgical intervention [1]. Although the lifelong incidence of this disease is approximately 7%–12%, the incidence of complications, such as plastron, gangrene, intra-abdominal abscess, and perforation, owing to delays in diagnosis and treatment varies between 20%–30% [2]. Despite the use of a complete history, physical examination, scoring systems, laboratory tests, and imaging methods in the diagnosis of AA, the negative exploration rates could go up to 20% even for experienced surgeons [3]. Nonetheless, the fact that delays in diagnosis and treatment lead to increased risk of perforation and further complications indicate the importance of accurately diagnosing AA [4].

The location and extent of the inflammatory processes of AA may vary depending on the location of the appendix. Although the location of the appendicular opening in the cecum base is a consistent anatomical feature, the same is not the case with its tail. Depending on the positional differences, the appendix may be retrocecal, subcecal, pre-ileal, ileoileal, and pelvic. Because these positional differences cause different symptoms, they may cause clinical confusion during the diagnosis of appendicitis [5]. The incidence of a retrocecal appendix varies between 26%–65%. In this position, right lower quadrant pain may not be present, and atypical findings, such as right upper quadrant pain, pararenal abscess, and a subhepatic abscess may be seen in 50% of the cases [6].

Several studies in the literature have used various inflammatory parameters, such as white blood cell (WBC), C-reactive protein (CRP), neutrophilia and neutrophil-to-lymphocyte ratio (NLR), and imaging methods like ultrasonography (USG) and abdominal computed tomography (CT) to differentiate between complicated and noncomplicated appendicitis [7,8]. However, no studies have analyzed the relationship between these parameters and appendiceal positions, as well as related complications. In our study, we investigated the diagnostic and prognostic significance of complete blood count parameters, such as WBC, MPV, NLR, and platelet-to-lymphocyte ratio (PLR), in retrocecal appendicitis, as well as the complications associated with appendicitis in this position.

Material and Methods

Study groups and study design

This study was carried out retrospectively at the tertiary university hospital after approval of the local ethics committee (approval number: 2019/06). Patients who were operated for AA between 1 July 2016 and 30 June 2019 were included in the study. After the power analysis, the number of patients to be included in the study groups was determined, and the study groups were formed as follows:

Antececal Appendicitis Group (n = 48): Patients who had antececal localization per the abdominal USG or CT results during the preoperative evaluation period, and antececal position during surgery were included in this group.

Retrocecal Appendicitis Group (n = 36): Patients who had retrocecal placement according to the abdominal USG or CT results during the preoperative evaluation period and retrocecal position during surgery were included in this group.

Control Group (n = 42): This group consisted of patients presenting with nonspecific abdominal pain to the emergency room, and was formed to assess the accuracy of the diagnostic tests.

Histopathological results were based on the definitive diagnosis of AA in both antececal and retrocecal appendicitis groups. In addition, patients were grouped as those with and without gangrenous histopathology per the observation or histopathology results and were analyzed for diagnostic tests. Patients under 15 years of age, pregnant women, patients with generalized peritonitis other than AA, acute or chronic systemic infection, concomitant diabetes mellitus, chronic obstructive pulmonary disease, cancer, and autoimmune diseases, patients who were given medical treatment before admission to the hospital and patients without preoperative USG or CT imaging were excluded from the study. In addition, patients with malignancy of the appendix were excluded from the study based on the histopathology results.

Complete blood count (CBC) and biochemical analysis

CBC and CRP analysis were performed on venous blood samples obtained from patients. Fully automatic devices were used for both analyses. NLR and PLR ratios were obtained using a simple calculation model.

Histopathological analysis

Surgical appendix samples were evaluated by a single pathologist. Specimens were grouped based on gangrenous histopathology and perforation.

Statistical analyses

All statistical analyses were performed using SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA). The data distribution was evaluated using the Kolmogorov-Smirnov test. Continuous variables were shown as the mean ± standard deviations, and categorical variables were shown as frequencies (n/ percentages). The significance of each difference between continuous variables was examined using the independent samples t-test or the Mann-Whitney U-test. The significance of each difference between categorical variables was compared using the Pearson's chi-squared test. Receiver operating characteristic (ROC) curve analysis was used to define the optimal cut-offs of the diagnostic tests, for which sensitivities, specificities, positive and negative predictive values, and area under the curve (AUC) were calculated. The Youden's index was used to optimize the accuracy of all calculations. A p-value of <0.05 was considered statistically significant.

Results

The mean age of the patients in the antececal appendicitis group was 24.2, while the mean age of the patients in the retrocecal appendicitis group was 30.8, and there was no difference between the groups (p=0.310). The gender distributions between the groups were similar. While the number of patients perforated in the anteecal appendicitis group was 9 (18.8%), it was 5 (13.9%) in the other group. The same values for gangrenous appendicitis rates were 13 (27.1%) and 10 (27.8%), respectively. No statistically significant difference was observed in rates of perforation and gangrenous appendicitis in both groups (p = 0.768 and p = 0.632, respectively).

The laboratory and radiological parameters used for diagnostic

purposes of the groups are compared in Table 1. The mean WBC, CRP, and NLR values were significantly higher in antececal and retrocecal appendicitis groups compared with the control group (p = 0.001 for retrocecal appendicitis versus control group, p < 0.001 for all other comparisons). Mean platelet volume (MPV) was significantly lower in the appendicitis groups compared with the control group (p < 0.001). No intergroup differences were observed regarding the mean PLR ratio. In addition, no differences were observed between antececal and retrocecal appendicitis groups for all tests. Moreover, no intergroup differences were noted regarding USG and CT (p = 0.193 for USG, p = 0.216 for CT).

ROC curves of laboratory and radiological data used to identify retrocecal appendicitis between the appendicitis groups are shown in Figure 1. Based on these data, the best sensitivity, specificity, PPD, NPD, and AUC values of NLR at a cut-off value of 9.09 were as follows: 83.33%, 35.42%, 49.20%, 73.90%, and 0.456, respectively. The same parametric values for the WBC at a cut-off level of 19000×10^9/L, were as follows: 25%, 89.58%, 64.30%, 61.40%, and 0.520. From the radiological point of view, the values for CT were 91.67%, 16.67%, 45.20%, 72.73, and 0.542, whereas the values for USG were 47.22%, 64.58%, 50%, 62%, and 0.559.

The data analysis performed to detect gangrenous histopathology in the retrocecal appendicitis group is given in Table 2. According to the data, no intergroup differences were noted regarding WBC, PLR, MPV, USG, and CT. Although the mean NLR was higher in the gangrenous appendicitis group, it was not statistically significant (p = 0.072). CRP levels were significantly higher in the gangrenous appendicitis group (p = 0.038). ROC curves of the same data are shown in Figure 2. Based on these data, the best sensitivity, specificity, PPD, NPD, and AUC values of NLR at a cut-off value of 3.31 were as follows: 100%, 41.67%, 46.20%, 100%, and 0.688, respectively. The same values for CRP at a cut-off level of 7.5 mg/L were 41.67%, 100%, 100%, 77.40%, and 0.714. The same parametric values for the WBC at a cut-off level of 13900×10^9/L were as follows: 58.33%, 66.67%, 46.70%, 76.20%, and 0.542. From the radiological point of view, the values for CT were 8.33%, 91.67%, 33.30%, 66.70, and 0.500, whereas the values for USG were 50%, 54.17%, 35.30%, 68.40%, and 0.521.

The data analysis performed to detect perforation in the retrocecal appendicitis group is given in Table 3. Per the data, no intergroup differences were observed regarding WBC, MPV, USG, and CT. Although the mean CRP was higher in the perforated appendicitis group, it was not statistically significant (p = 0.066). Mean NLR and PLR values were significantly higher in the perforated appendicitis group (p = 0.003 for NLR and p = 0.001 for PLR). ROC curves of these parameters are shown in Figure 3. According to these values, the best sensitivity, specificity, PPD, NPD, and AUC values of NLR at a cut-off value of 8.89 were 80%, 90.32%, 57.10%, 96%, and 0.890, respectively. The same values for PLR at a cut-off value of 225 were 80%, 100%, 100%, 96.90%, and 0.923, whereas for CRP at a cut-off value of 7.5 mg/L were 60%, 93.55%, 60%, 93.50%, and 0.758. From the radiological point of view, the values for CT were 20%, 93.55%, 33.30%, 87.90, and 0.568, whereas the values for USG were 60%, 48.39%, 15.80%, 88.20%, and 0.542.

Table 1. Comparison of demographic data of groups

Parameters	Antececal app. Group (n=48)	Retrocecal app. Group (n=36)
Age (year)	2.42±12.35	30.89±9.80
Gender (F/M) (n)	17/31	20/16
Perforation (n/%)	9 (%18.8)	5 (%13.9)
Gangrenous appendicitis rate(n/%)	13 (%27.1)	10 (%27.8)

(Abb: app.: appendicitis, F: female, M: male, WBC: White blood count, CRP: C-reactive protein, NLR: neutrophil-lymphocyte ratio), PLR: platelet-lymphocyte ratio, MPV: mean platelet volume   [Age]p=0.310

Table 2. Comparison of laboratory data of groups

Parameters	Antececal app. Group (n=48)	Retrocecal app. Group (n=36)	Control Group (n=42)
WBC (x10⁹/L)	14410±4803.18*	14678±4667.35*	8227.6±1876.49
CRP (mg/L)	4.80±6.99*	3.32±5.16#	0.36±0.37
NLR	7.63±5.2*	6.61±4.39*	3.48±2.54
PLR	165.92±120.27	157.43±113.16	151.98±111.01
MPV (fL)	7.37±1.05*	7.58±1.52*	9.04±1.04
USG (n/%)	17 (35.41%)	17 (47.22%)	N/A
CT (n/%)	40 (83.33%)	33 (91.67%)	N/A

(Abb: app.: appendicitis, WBC: White blood count, CRP: C-reactive protein, NLR: neutrophil-lymphocyte ratio PLR; platelet) lymphocyte ratio, MPV: mean platelet volume, USG: ultrasonography, CT: computed tomography
*p<0.001 vs. control group, p=0.001 vs. control group
[USG]p=0.193, [CT]p= 0.216

Table 3. Accuracy rates of laboratory and radiological data for demonstrating retrocecal appendicitis

Data Index	Sensitivity (%)	Specificity (%)	PPD	NPD (%)	AUC (%)	Cut-off	Youden's
WBC (x10⁹/L)	25.00	89.58	64.30	61.40	0.520	19000	0.146
CRP (mg/L)	63.89	60.42	54.80	69.00	0.589	1.36	0.243
NLR	83.33	35.42	49.20	73.90	0.544	9.09	0.187
PLR	83.33	29.17	46.90	70.00	0.522	184	0.125
MPV (fL)	69.44	45.83	49.00	66.70	0.540	7.06	0.153
USG	47.22	64.58	50.00	62.00	0.559	N/A	0.118
CT	91.67	16.67	45.20	72.73	0.542	N/A	0.083

Abb: NPV: negative predictive value, PPV: positive predictive value, AUC: area under a ROC curve, WBC: White blood count, CRP: C-reactive protein, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, MPV: mean platelet volume, USG: ultrasonography, CT: computed tomography

Discussion

In this study, we investigated the relationship between NLR and the position of the appendix in AA and the diagnostic value of NLR in identifying gangrene and perforation in retrocecal appendicitis. Consequently, we determined that NLR has no diagnostic value in identifying antececal and retrocecal appendicitis but has a diagnostic value in detecting gangrenous histopathology and perforation in retrocecal appendicitis.

AA is one of the most common causes of emergency surgery. The diagnosis of AA is typically made based on physical examination and disease-specific anamnesis. Although technological and radiological advances have improved the diagnosis accuracy and negative appendectomy rates, the diagnostic process is still complicated in some cases. Delays in the diagnosis and treatment of AA lead to gangrene and perforation. Therefore, early diagnosis of AA is crucial for minimizing morbidity and mortality by reducing the development of gangrene or perforation [3,9]. On the other hand, some studies have revealed that antibiotic treatment is safe in uncomplicated appendicitis,
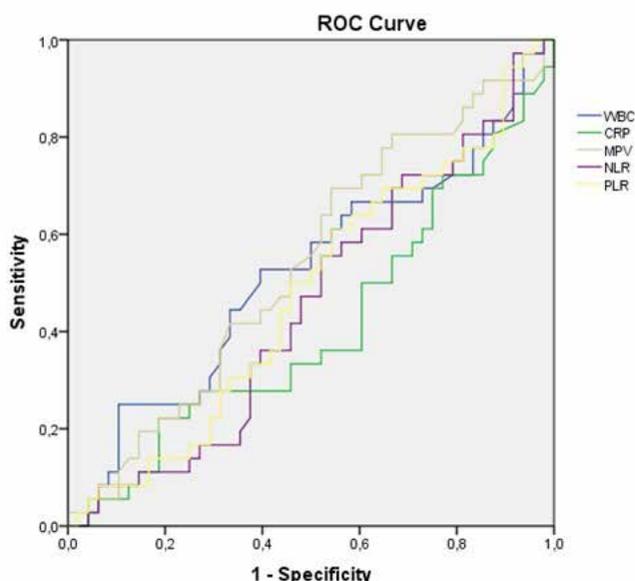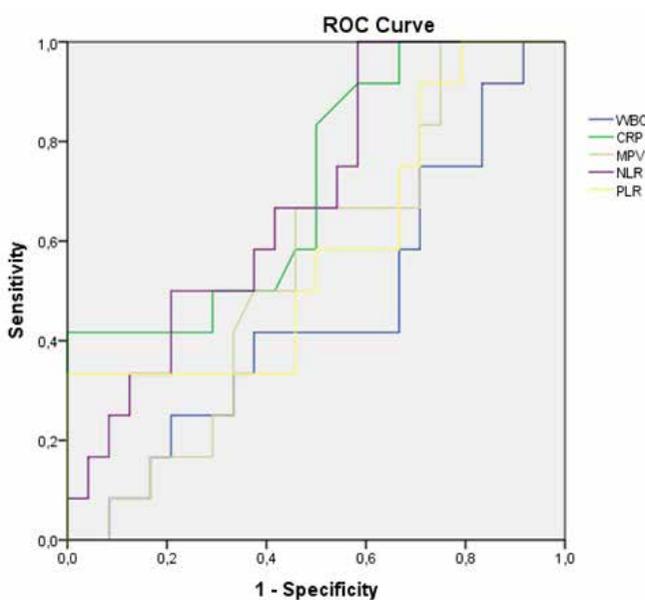
Figure 1. ROC analysis between appendicitis groups

Figure 2. ROC analysis of data in the retrocecal appendicitis group to demonstrate gangrenous histopathology.
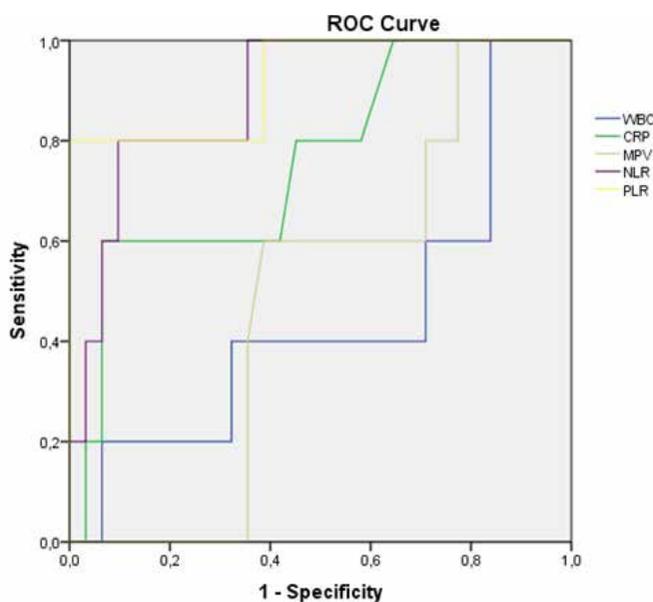

Figure 3. ROC analysis of data in the retrocecal appendicitis group to demonstrate perforation

and therefore, it is vital to distinguish between complicated and uncomplicated appendicitis to avoid unwarranted surgery in patients suitable for medical treatment [10]. However, the disadvantage lies in the cost of advanced tests applied to increase diagnosis rates.

Increased WBC, the earliest sign of appendiceal inflammation reported in various studies, is a widely used test in the diagnosis of AA. Notably, its sensitivity and specificity are distributed over a wide range [3]. The sensitivity of WBC with a cut-off value greater than 10000–12000 × 109/L varies between 65% and 85%, and its specificity varies between 32% and 85% [11]. In a meta-analysis involving approximately 3382 patients and 14 studies, the sensitivity and specificity for WBC > 10000 × 109/L were 83% and 67%, respectively [11]. Therefore, the use of WBC as a reliable parameter in the diagnosis of AA is controversial. However, the study of Atema et al. [12] that evaluated the diagnostic value of the number of WBCs in complicated and uncomplicated appendicitis reported that WBC levels of greater than 13000 × 109/L alone did not effectively predict the incidence of perforation, but could contribute when used in combination with other parameters. However, no data in the literature provide information about the position of the appendix. In our study, we found that WBC was significantly higher in both antececal and retrocecal appendicitis compared with the control group. We detected low sensitivity, specificity, and AUC values even at cut-off values of WBC > 19000 × 109/L (25%, 89.58%, and 0.520%, respectively) in AA with a high complication rate and low probability of diagnosis. In addition, we determined that for retrocecal location WBC had no significant efficacy in detecting gangrene development and perforation.

Another common inflammatory marker used in the diagnosis of AA is CRP. CRP is an acute-phase reactant that increases with the progression of inflammation in several diseases. A recent meta-analysis observed that the diagnostic accuracy rates of CRP have a wide range [13]. In a meta-analysis performed by Hallan et al. [14], the sensitivity and specificity of high CRP values were between 40% and 99% and 27% and 90%, respectively. Moon et al. [15] determined that elevated CRP values were associated with complicated appendicitis. Aydin et al. [16] observed that the sensitivity of CRP was 53.3%, and the specificity was 67% in complicated appendicitis. Some studies have indicated that compared with leukocytosis, a CRP above 5 could be a significant factor in differentiating complicated and noncomplicated AA [17]. In our study, we determined the sensitivity and specificity of CRP in retrocecal appendicitis as 63.89% and 60.42%. We observed that elevated CRP values might be associated with gangrene formation, but provide no details regarding perforation.

Apart from WBC and CRP, NLR is another indicator used as a diagnostic marker in inflammatory diseases. Neutrophilia and lymphocytopenia are components of cellular response in systemic inflammation. The increase in the difference between the numbers of neutrophil and lymphocyte reflects the severity of the inflammatory response. NLR, which indicates this difference, has therefore been used as a diagnostic and prognostic marker in several inflammatory pathologies [18]. Notably, NLR is not a new marker in the diagnosis of AA. The

argument that NLR is a more sensitive parameter than leukocyte counts was presented by Goodman et al. [19] 20 years ago. In recent years, more and more comprehensive studies have been published. Shimizu et al. [20] identified that the sensitivity and specificity of NLR are 44% and 22% for diagnosing AA at a cut-off value of >5. Ishizuka et al. [21] detected that the sensitivity and specificity of NLR are 73% and 39%, at a cut-off value of >8, in the differentiation of complicated and uncomplicated appendicitis. Kahramanca et al. [22] reported two cut-off values for NLR, namely 4.68 (65% sensitivity, 55% specificity) and 5.74 (71% sensitivity, 49% specificity), to distinguish AA from the normal appendix, and complicated appendicitis from uncomplicated appendicitis, respectively. Sevinc et al. [23] noted that cut-off values of NLR were 3.0 (81% sensitivity, 53% specificity) and 5.5 (78.4% sensitivity, 41.7% specificity) for the diagnosis of AA and perforated appendicitis, respectively. In another study, Yardimci et al. [9] suggested that NLR is a significant parameter in detecting complications, such as gangrene and perforation, in AA. In our study, NLR levels were significantly higher in the AA group, concordant with the data in the literature. Our study detected the sensitivity and specificity of NLR to be 83.33% and 35.42%, respectively. In addition, the sensitivity and specificity were 100% and 41.67% for detecting gangrenous histopathology in retrocecal appendicitis. Perforation is a comparatively stronger indicator among parameters, with its sensitivity and specificity determined to be 80% and 90.32%, respectively.

Platelet count is part of CBC and is one of the most commonly used laboratory tests. The platelet-associated CBC parameters are platelets, MPV, and platelet distribution width. Among these parameters, MPV, which shows platelet function and activation, is the best known, and recent studies have revealed that it can be used as a diagnostic test in several inflammatory diseases [3,24]. Tanrikulu et al. [24] noted that MPV was significantly lower in cases of appendicitis compared with a normal appendix. Kim et al. [25] described MPV as an independent risk factor associated with mortality in patients with sepsis. Previous studies that investigated the diagnostic value of MPV in AA have reported cut-off values of MPV between 7.3 and 7.95 [3,24]. In our study, MPV values were noted to be significantly lower in the AA groups compared with the control group, and cut-off values were concordant with the literature. However, no significant differences based on MPV levels were observed for distinguishing between antececal and retrocecal appendicitis. In addition, MPV levels had no clinical significance in detecting gangrenous histopathology and perforation in retrocecal appendicitis. Based on the recently used PLR, no differences were noted between appendicitis and control groups. Although PLR values were significantly higher in the gangrenous group of retrocecal appendicitis compared with the non-gangrenous group, it was not statistically significant. However, in the perforated appendicitis group, the sensitivity, specificity, and AUC values of PLR at a cut-off value of >225 were 80%, 100%, and 0.923, respectively.

Conclusion

The CBC parameters, including WBC, CRP, NLR, and MPV, can be used as a diagnostic test in acute appendicitis, but none of these parameters can differentiate between antececal and retrocecal appendicitis. We identified that CRP and NLR might be useful for detecting gangrenous histopathology, and NLR and PLR might aid in detecting perforated appendicitis. Therefore, we consider that NLR and PLR could be used as an essential prognostic indicator, especially in cases with atypical plugs and retrocecal appendicitis, as seen on CT or USG.

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